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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

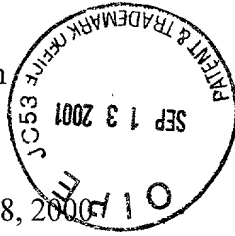
In re Application of:

T. Crompton

Serial No: 09/724,964

Filed: November 28, 2000

For: Methods and Compositions for  
Regulating Lymphocyte Activity



Attorney Docket No. CIBT-P01-080

Art Unit: Not yet assigned

Examiner: Not yet assigned

**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

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September 10, 2001

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and of Mail Deposit

  
Karen DiRocco

Assistant Commissioner of Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

This amendment is being filed in reply to the outstanding Notice to Comply, mailed August 20, 2001, in connection with the above application. Please enter the following amendments:

**In the specification:**

Please replace the paragraph from lines 23-29 on page 39 with:

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5'-gcgcgcttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-  
GAGGAAatcgatgcgcgc (primer 1) (SEQ ID No. 23)

5'-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACCCGCCGCGCG-  
CACTCGgatccgcgcgc (primer 2) (SEQ ID No. 24)

Please replace the paragraph from lines 10-29 on page 40 with:

Individual colonies are selected, cut with *AsuII* and *BamHI*, and the size of the *AsuII/BamHI* fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, an cut with *AsuII* and *BamHI* to produce the gene activation construct

cgaagcgaggcagccagcgagggagagagcgagcgggcgagccggagcgaggaaATCGAAGGTTCTGAATCCTTC  
CCCCACCACCATCACTTTCAAAAGTCCGAAAGAATCTGCTCCCTGCTTGTGTGTTGG  
AGGTCGCTGAGTAGTGC GCGAGTAAAATTTAAGCTACAACAAGGCAAGGCTTGACC  
GACAATTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCGATGTA  
CGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATT  
ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA  
AATGGCCCGCCTGGCTGACCGCCCAACGACCCCGCCCATTTGACGTCAATAATGAC  
GTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTA  
TTTACGGTAAACTGCCCACCTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC  
CCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGAC  
CTTATGGGACTTTTCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG  
GTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGA  
TTTCCAAGTCTCCACCCCATTTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAA  
CGGGACTTTCCAATAATGTCGTAACAACCTCCGCCCCATTGACGCAAATGGGCGGTAG  
GCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCA  
CTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTTGGT  
ACCGAGCTCGGATCgatatgggaaagcgcaagagagagcgacacgcacacccgcccgcgcactcgg (SEQ ID  
No. 25)

Please replace the first paragraph on page 53 with:

In an illustrative embodiment, the *ptc* therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCGCCGCGCGTCGCC (SEQ ID No. 26)

5'-TTCCGATGACCGGCCTTTCGCGGTGA (SEQ ID No. 27)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID No. 28)

*The replacement paragraphs presented above incorporate changes as indicated by the marked-up versions below.*

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5'-gcgcgcttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgcgc (primer 1) (SEQ ID No. 23)

5'-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACCCGCCGCGCG-CACTCGgatccgcgcgc (primer 2) (SEQ ID No. 24)

Individual colonies are selected, cut with *Asu*II and *Bam*HI, and the size of the *Asu*II/*Bam*HI fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, an cut with *Asu*II and *Bam*HI to produce the gene activation construct

cgaagcgaggcagccagcgagggagagagcgagcgggagcgagccggagcgaggaaATCGAAGGTTCTGAATCCTTC  
CCCCACCACCATCACTTTCAAAGTCCGAAAGAATCTGCTCCCTGCTTGTGTGTTGG  
AGGTCGCTGAGTAGTGCGCGAGTAAAATTTAAGCTACAACAAGGCAAGGCTTGACC  
GACAATTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCGATGTA  
CGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATT  
ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCGCGTTACATAACTTACGGTA  
AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGAC  
GTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTA  
TTACGGTAAACTGCCCCTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC  
CCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGAC  
CTTATGGGACTTTCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG  
GTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGA  
TTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAA  
CGGGACTTTCCAAAATGTCGTAACAACCTCCGCCCCATTGACGCAAATGGGCGGTAG  
GCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCA  
CTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTTGGT  
ACCGAGCTCGGATCgatctgggaaagcgcaagagagagcgcacacgcacacccgcccgcgcgactcgg (SEQ ID  
No. 25)

In an illustrative embodiment, the *ptc* therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCCGCCGCCGTCGCC (SEQ ID No. 26)

5'-TTCCGATGACCGGCCTTTCGCGGTGA (SEQ ID No. 27)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID No. 28)

### REMARKS

Applicants submit herewith an amended sequence listing including the sequences noted by the Examiner. Pursuant to the Rules, a hard copy of the sequence listing and a computer readable form of the sequence listing (the diskette) are submitted herewith.

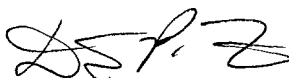
I state that this submission, filed in accordance with 37 C.F.R. 1.821(g) does not include new matter. I further state that the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. 1.821(c) and (e), respectively, are the same.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

Date: September 10, 2001

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